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7590 KEVIN E. MC VEIGH RHODIA INC. 259 PROSPECT PLAINS RD. CRANBURY, NJ 08512			EXAMINER LAO, MARIALOUISA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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DETAILED ACTION

Response to Arguments

1. Applicant's arguments, see REMARKS, filed 7/27/07, have been considered as follows
 - a. with respect to the rejection(s) of claim(s) 5-6 under 35 U.S.C. 112 2nd ¶ have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.
 - b. with respect to the rejection(s) of claim(s) 1-18 under 35 U.S.C. 112 1st ¶ have been fully considered and are not persuasive. Applicants amended the claims to encompass a Markush list of bases, for which there is no support in the specification. Therefore, the rejection has been maintained.
 - c. with respect to the rejection(s) of claim(s) 1, 2, 7, 8 & 19 and 1-22 under 35 U.S.C. 102/103 2nd ¶ have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

However, upon further consideration, a new ground(s) of rejection is made as discussed below.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Claims 1-18 are rejected** under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a base, **like potassium hydroxide and potassium carbonate**, does not reasonably provide enablement for "*alkaline earth carbonate, bicarbonate, sulfonate or phosphonate*". The specification does not enable the person skilled in the art of synthetic

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chemistry, to make the invention commensurate in scope with these claims. The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in the art, g) the predictability or unpredictability of the art, and, h) the breadth of the claims.

In the present case, the important factors leading to a conclusion of lack of scope of enablement are the absence of any working example of alkaline earth carbonate, bicarbonate, sulfonate or phosphonate, the quantity of experimentation necessary, and the broad scope of the claims.

a) the quantity of experimentation necessary. Since there are at least 6 elements in the alkaline earth metal family and four form variations (i.e. carbonate, bicarbonate, sulfonate or phosphonate) in which these could be in, the permutation of combinations and subcombinations to be tested are proportionately numerous.

b) the amount of direction or guidance presented. The instant specification in pages 14-15 provides guidance for using alkali earth metal hydroxide and carbonates (KOH and K_2CO_3), but not for alkaline earth metal salts as bases for the arylation method described in the instant claims.

c) the presence or absence of working examples. There are no working examples of alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate. The two examples, directed to potassium hydroxide and potassium carbonate, presented in pages 14-15 of the specification are found atypical of the purported nature of the base as recited in the claims; since potassium belongs to the alkali earth metals.

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d) the nature of the invention. The nature of the invention falls under a general category of known chemical processes.

e) the state of the prior art. The prior art (US6335463, US'463) shows the use of alkali earth metal salts as bases in an arylation synthesis.

f) the relative skill of those in the art. The persons of ordinary skill in the art at the time of the invention would be synthetic organic chemists.

g) the predictability or unpredictability of the art. Catalysts are unpredictable. Thus, the processes dependent thereto, would likewise proceed in an unpredictable manner; since a catalyst that is efficacious for an epoxidation process may not predictably behave the same way in a hydrogenation process.

h) the breadth of the claim. Claim 1 is broad since it encompasses the plurality of all alkaline earth carbonate, bicarbonate, sulfonate or phosphonate.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/use the full scope of the claimed invention without undue experimentation. In re Wright 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed.Cir.1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 2, 7, 8, and 19 are rejected under 35 U.S.C. 103(a) as obvious over Sommer (US6335463, US'463) in view of Goodbrand et al. (US548542, US'542).

Applicant Claims

8. The instant claims are drawn to a method of arylating a nucleophile, comprising reacting the nucleophile with a substrate aromatic compound, ArX, in the presence of a copper catalyst, a base and water, wherein Ar=aryl, heteroaryl or alkenyl; X=halo, sulfonate or phosphonate, base comprises an alkaline earth carbonate, bicarbonate, hydroxide or phosphate and the copper catalyst comprises a copper atom or ion and a ligand. Further the nucleophile comprises a HN-containing heterocycle or a HN-containing compound, described in the claims, as recited.

The instant claims recite potassium hydroxide or potassium carbonate as suitable bases for arylation.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

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9. US'463 in claims 1, 3 and 4 column 8 lines 27-59 and 63-67 and in claim 33 column 10 lines 46-48, recites a method of arylating a nucleophile, which encompasses the reaction in the presence of a copper catalyst, a base and water, where the nucleophile is N-(4-fluorophenyl)glycine, wherein correspondingly in the instant claims, this compound fits the HN-containing compound according to the formula $\text{HN}(\text{R}_1)\text{R}_2$, wherein $\text{R}_1 = \text{aryl}$ and $\text{R}_2 = \text{R}_3\text{-C(=O)-}$ and $\text{R}_3 = \text{-OR}_5$; and, the aromatic compound is dichlorobenzoic acid, wherein correspondingly in the instant claims, this compound fits ArX , $\text{Ar} = \text{aryl}$, phenyl ring, which is substituted, other than the X substituent in addition to the X substituent, on one or more carbons of the ring (herein, the substituents are -Cl , COOM_1) and $\text{X} = \text{halo}$. Albeit the reacting compounds are alkali metal salts, these are the same alkali metals as the base compounds (see column 9 claim 10), US'463 states that the alkali metal salt forms of the reacting compounds render a more efficacious reaction to proceed.

10. US'463 in column 5 Example 1 teaches that the copper catalyst is present at 4mole%, the ArX is at 2.1 equivalents relative to the nucleophile and in column 4 lines 38-39, the amount of water is minimally present. The base is potassium carbonate.

*Ascertainment of the Difference
Between Scope of the Prior Art and the Claims
(MPEP §2141.012)*

11. US'463 differs from the instant claims in its silence with the catalyst comprising copper and *inter alia*, a ligand. US'542 is relied upon to show (see Abstract) arylamine processes which comprise the reaction of an aniline and a haloaromatic component in the presence of a ligand copper catalyst, and wherein the ligand is selected from the group consisting of tertiary amines.

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***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

12. It would be obvious to one skilled in the art at the time of the invention to start with the method of US'463 to arylate a nucleophile and couple this with the catalyst of US'542, since the catalyst of US'542 are used for arylamine processes.

One having ordinary skill in the art would have been motivated to use a ligand copper catalyst since these are equivalent to a copper catalyst comprising, *inter alia*, an atom or ion and a ligand; and the artisan, by routine practice due to cost and availability, would reach a reasonable degree of success as in the instant application.

13. Thus, the combination of the teachings of the cited prior art references is fairly suggestive of the *prima facie* obviousness of the instant claims.

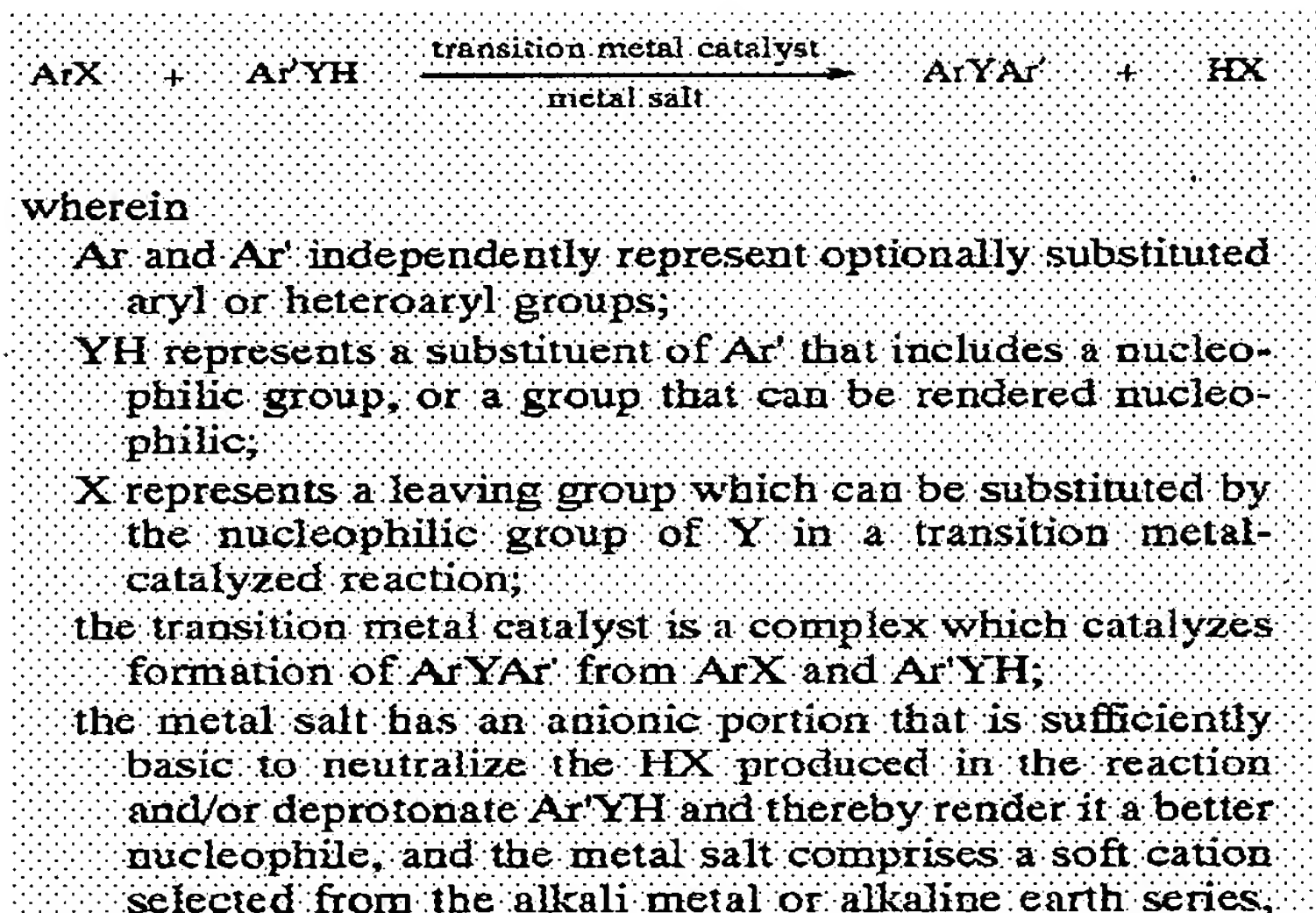
14. **Claims 1 -22 are rejected** under 35 U.S.C. 103(a) as obvious over Marcoux et al. (US6395939, US'939) and further in view of Zanon et al. (US2005/0101788, US'788) and Sommer (US6335463, US'463), further in view of Goodbrand et al. (US548542, US'542).

15. The instant claims are drawn to a method of arylating a nucleophile, comprising reacting the nucleophile with a substrate aromatic compound, ArX, in the presence of a copper catalyst, a base and water, wherein Ar=aryl, heteroaryl or alkenyl; X=halo, sulfonate or phosphonate, base comprises an alkaline earth carbonate, bicarbonate, hydroxide or phosphate and the copper catalyst comprises a copper atom or ion and a ligand. Further the nucleophile comprises a HN-containing heterocycle or a HN-containing compound, described in the claims, as recited.

16. The instant claims recite potassium hydroxide or potassium carbonate as suitable bases for arylation.

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17. US'939 discloses in column 2 lines 33-58, an arylation synthesis that encompasses the reaction as shown:



wherein, correspondingly in the instant claims, the arylation takes place between the aromatic compound= ArX and the nucleophile= Ar'YH in the presence of a base and copper catalyst.

18. US'939 discloses a typical example of the reaction supra in column 19 scheme 6 lines 33-48 with the reaction of 3-bromoquinoline and N-methylaniline.

19. US'939 also discloses the typical Copper catalysts in column 23 lines 11-60, which include copper ion sources.

20. Albeit, US'939 does not expressly disclose specific substituents for ArX and Ar'YH and the copper catalyst comprising, *inter alia*, a ligand; and the use of base and water, US'788, US'463, US'542 are relied upon to answer these deficiencies.

21. US'788 discloses in page 8 claim 1 that sertindole can be manufactured with the reaction of 5-chloroindole, which is a nucleophile and HN-containing compound, with 4-fluorophenylhalide, which is an aromatic halide, in the presence of a base, a chelating ligand and

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copper catalyst. In page 2 section[0021], US'788 states that the chelating agent is the compound of the formula $X-(CR_1R_2-(CR_5R_6)_n-CR_3R_4-Y)_m$, which read on the ligand of instant claims 13 and 14, when X and Y = NR_7R_8 and R_7 and R_8 are independently H, C1-6 alkyl; when $n=0,1,2,3$ and R_1-R_9 independently are selected from hydrogen, C1-6 alkyl, C1-6 aryl; when $m=1$.

22. While US'463, described in detail supra under claim rejections under 35USC 103, teaches the use of water in an arylation method to produce sertindole and US'542 teaches the ligand copper catalyst in arylamine processes.

23. US'788 discloses in page 2 [0025] the use of alkali earth metals like potassium and sodium carbonates; but does not disclose alkaline earth metal carbonate, bicarbonate, sulfonate or phosphonate.

24. It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to employ the specific compounds, 5-chloroindole with 4-fluorophenylhalide of US'788 and the water in US'463 and the ligand copper catalyst of US'542, and the reaction parameters thereto and therewith, using the alkali salts as bases in the arylation method of US '939 since the compounds and parameters are applicable for equivalent types of arylation methods and these compounds fit the definition profiles of a nucleophilic compound and an ArX , respectively and the parameters (i.e. base and water and ligand Cu catalyst), as in the parameters recited in the instant application using the equivalent alkali salts as bases, with water and a Cu catalyst, comprising atom, ion and a ligand.

25. One having ordinary skill in the art would have been motivated to do combine the teachings of US'788, US'463, US'939 and US'542, since the arylation methods are essentially

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the same and equally employ compounds and reaction parameters that are equivalent as defined in the instant application and the artisan would have expected a reasonable degree of success.

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to have yielded predictable results to one of ordinary skill in the art at the time of the invention.

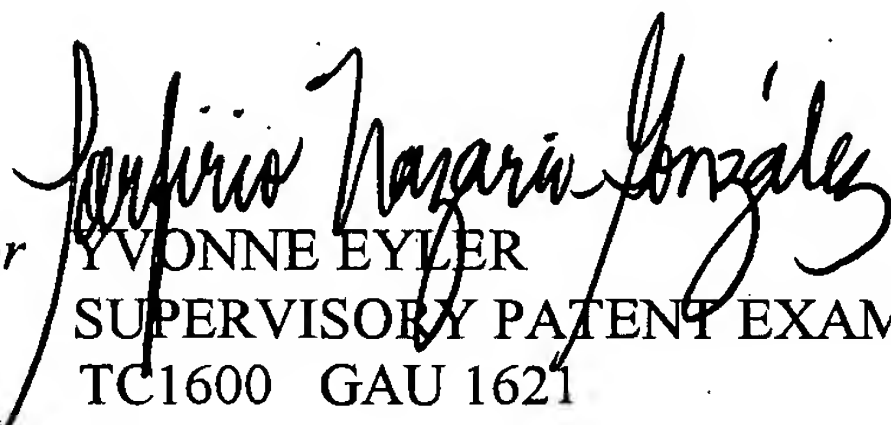
26. Thus, the combined teachings of the cited prior art references render the instant claims, as recited, unpatentable.

27. No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MLouisa Lao whose telephone number is 571-272-9930. The examiner can normally be reached on Mondays to Thursdays from 8:00am to 8:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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